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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,714	01/14/2000	YECHIEL SHAI	SHAI=2	4669

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	22

DATE MAILED: 06/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/367,714	Applicant(s) SHAI ET AL.	
	Examiner David Lukton	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/19/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,20,21,27-35 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,20,21 and 27-34* is/are rejected.

7)☒ Claim(s) *35 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Pursuant to the directives of paper No. 21 (filed 3/19/01), claims 15-17, 36 have been cancelled, claims 1, 2, 6, 7, 9, 11-14, 20, 21, 34, 35 amended, and claim 37 added. Claims 1-14, 20, 21, 27-35, 37 are pending.

*

Claims 1-14, 20, 21, 27-33 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 recites in part (B), the following:

  "a corresponding amino acid sequences comprising only L amino acids residues is not found in nature"

  What is meant by "corresponding"...? Does this mean that the two peptides are absolutely identical in all respects other than in the stereochemistry of the *alpha*-carbon...?

- Claim 14 is not properly dependent on claim 1. Claim 1 excludes all peptides which consist solely of L-amino acids. In claim 14, SEQ ID NO: 95 consists of L-amino acids.

- Claim 31 recites inhibition of a "viral activity". Which activities are intended?

*

Claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by Shai (*J. Biol. Chem.* **271**, 7305, 1996).

As indicated previously, Shai teaches (p. 7308, col 1, 1st paragraph) that the peptide

designated " (D)$P^7L^{18}L^{19}$ " is antibacterial but non-hemolytic.

In response to this, applicants have first argued (paper No. 18, filed 10/3/01) that the peptide designated " (D)$P^7L^{18}L^{19}$ " is the same as peptide #16 that is presented on page 26 of the instant specification, as well as in table I (pages 29-30). However, this does not appear to be true. According to the sequence listing, the C-terminal residue of SEQ ID NO:16 is glutamine, nothing more, and nothing less. By contrast, the C-terminal residue of the peptide designated " (D)$P^7L^{18}L^{19}$ " is not glutamine *per se*, but is instead glutamic acid in which both of the carboxyl groups are replaced with the following:

$$-CO-NH-CH_2-CH_2-NH_2$$

Second, applicants have argued that this peptide does not fall within the scope of the claims because if one were to replace each of the D-amino acids with L-amino acids, the result would be a peptide that is found in nature. However, this is not correct. The N-(ethylenediamine)-amide group is not naturally occurring, at least for this peptide. Third, applicants have argued that in table 1 of the instant specification, data is presented which shows that the SEQ ID NO:16 is hemolytic. However, applicants assertion on this point is contrary to what is conveyed in table 1. In further arguing that SEQ ID NO:16 is hemolytic, applicants are requested to be much more detailed in their explanation.

The rejection is maintained.

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The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 2, 7-11, 20, 34 are rejected under 35 U.S.C. §103 as being unpatentable over Maloy (U.S.P. 5,792,831).

As indicated previously, Maloy teaches cytolytic peptides containing D-amino acids. In traversing, applicants have argued (paper No. 18, filed 10/3/01) that for each of the disclosed peptides, if one were to replace each of the D-amino acids with L-amino acids, the result would be a peptide that is found in nature. This is found unpersuasive for at least four separate reasons. First, setting aside the issue of "D" versus "L" amino acids, most of the dislcosed peptides are not naturally occurring. It may be true that each genus includes one or two peptides which <u>are</u> naturally occurring (again setting aside the issue of

"D" versus "L" amino acids), but in the vast majority of disclosed peptides, the amino acid sequence differs by at least one amino acid from any that is naturally occurring.

The second point is that Maloy also discloses (col 2, line 42+) that the indole nitrogen of a tryptophanyl residue can be formylated, and that the phenyl group of phenylalanine can be iodinated. Thus, any peptide in which the indole nitrogen of Trp is formylated, or in which the phenyl group of Phe is iodinated would meet the requirement of being "non-natural".

The third point is that there are modifications to amino acid sidechains for which one of ordinary skill would expect no adverse effect on activity. Primarily this includes extending the side chain by one methylene unit. For example, replacing a phenylalanine with a phenethylglycine, or replacing an alanine with ethylglycine or replacing a lysine with a pentylaminoglycine would result in a peptide that one would expect, *a priori*, to exhibit the same activity as the unmodified peptide [*In re Shetty* (**195** USPQ 753) and *In re Hass & Susie* (**60** USPQ 544)].

Fourth, there is the matter of the "random copolymer" [part (C) of claim 1]. The issues raised by this are at least as much within the field of probability and statistics as they are within the field of chemistry. For example, there is a finite probability that if one "flips" a coin 10 times, it will come up "heads" all 10 times. One can calculate the odds of this happening, but when it does happen, it is "random". The term "random" is <u>not</u> interpreted

to mean that, for a system in which "n" events are possible (at any one given point in time), and wherein each of those "n" events is permitted to occur "m" times, that each of those events will occur "m/n" times. To use the example of the coin toss, a "random" distribution of heads versus tails is not necessarily limited to exactly 5 heads and 5 tails (for the example of 10 tosses), but a "random" event would include, e.g., 8 heads and 2 tails, or even 10 heads and 0 tails. There is also the matter of the "order" of the events. To continue with the coin toss example, if one "flips" a coin 10 times, there is the possibility of 5 heads/5 tails, of course. But for the case of 5 heads/5 tails, there are numerous possibilities with regard to the ordering of the events. For example, for the case of 5 heads/5 tails, each of the following is possible ("H" = heads, "T" = tails):

H-T-H-T-H-T-H-T-H-T

H-T-T-T-T-H-T-H-H-H

H-T-T-T-T-T-H-H-H-H

T-T-T-H-H-H-H-H-T-T

All of these can be considered "random" sequences, since there is a finite probability that any one of them would occur.

Consider, e.g., the peptides disclosed in col 8, line 28+ of Maloy. Suppose one were to prepare N-carboxyanhydrides of each of the following four amino acids, and that all four of them were combined together in a reaction vessel: Ser, Lys, Ala, and Phe. The fact

is that there is a finite probability that any of the peptides in col 8, line 28+ could be formed.

Thus, for each of the foregoing reasons, the claims are rendered obvious.

*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton. Phone: (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600